REMARKS

Claims 1-37 are pending. Claims 2, 3, 5, 19-22, and 34-36 are withdrawn from consideration.

Rejections Under 35 U.S.C. § 103

Claims 1, 4, 6-18, 23-33, and 37 are rejected under 35 U.S.C. § 103 as being unpatentable over Maciaszek et al. (Journal of Virology, 1998, Vol. 72, No. 7, pp. 5862-69) in view of Gander et al. (U.S. 4,323, 581). Applicants respectfully disagree for all the reasons previously presented and for the reasons presented below.

Claims 1, 4, and 6-18 are directed to methods of "inhibiting viral infection in a subject." Claims 23-33 and 37 are directed to methods of "inhibiting a viral attachment/entry or exit phase of a virus." Maciaszek et al. and Gander et al. fail to teach or suggest methods of "inhibiting viral infection" or "methods of inhibiting viral attachment/entry or exit phase of a virus" and, therefore, Applicants request the that rejection be withdrawn.

In particular, Maciaszek et al. teaches that retinoic acid repressed HIV-1 replication in undifferentiated monocytes. See, e.g, Maciaszek et al., Abstract. However, this is not the same as teaching inhibition of viral infection or inhibition of viral entry. Moreover, Maciaszek et al. specifically teaches that retinoic acid treatment was only effective if administered during differentiation and not after differentiation.

> Addition of physiological concentrations of retinoids, either retinol or retinoic acid, during differentiation results in MDMs that are nonpermissive for HIV-1 replication. **However, retinoid treatment after this critical period has no effect on virus replication**. (Maciaszek et al. at page 5866, right hand column) (emphasis added).

Claim 37 is directed to: "The method of claim 28, wherein the cell is a differentiated macrophage." At the minimum, Maciaszek et al. cannot render claim 37 obvious. Indeed, Maciaszek et al. specifically teaches away from the method of claim 37. Moreover, this teaching of Maciaszek et al. is conclusive evidence that Maciaszek et al. cannot and does not teach or

suggest the claimed method of "inhibiting viral infection in a subject" because a subject has differentiated macrophages which Maciaszek et al. acknowledges will become infected regardless of retinoid treatment.

Furthermore, at the time of invention a person of skill in the art would not have had any reasonable expectation of success because of the contradictory teachings of the prior art. This is evidenced, at least, by J. A. Turpin et al., Enhanced HIV-1 replication in retinoid-treated monocytes. Retinoid effects mediated through mechanisms related to cell differentiation and to a direct transcriptional action on viral gene expression, *Journal of Immunology*, vol. 148, pages 2539-2546 (submitted herewith). Turpin et al. clearly teaches away from the Applicants' method because Turpin et al. teaches that retinoid enhances viral replication. See e.g., Turpin et al., Abstract and the last sentence of the Discussion on page 2545. In light of Turpin et al. a person of skill in the art would not have had any reasonable expectation of success. The contradictory nature of the art is also evidenced by Maciaszek et al.'s acknowledgement that "vitamin A intake of >20,000 IU/day increased the relative risk of AIDS mortality." See Maciaszek et al. page 5862, right column. In light of the totality of the prior art, a person of skill in the art would not have expected retinoids to inhibit viral infection. In contrast, Applicants made the unexpected observation that N-4-(hyroxyphenyl)retinamide modulated ceramide metabolism resulted in the inhibition of viral infection and the inhibition of viral entry. Importantly, Applicants' method is not directed to retinoids per se but rather is directed to ceramide-generating retinoid and particularly N-4-(hyroxyphenyl)retinamide.

In sum, Maciaszek et al. and Gander et al. fail to teach or suggest Applicants' claimed methods. Accordingly, Applicants respectfully request that the rejection be withdrawn.

CONCLUSION

It is believed the application is in condition for immediate allowance, which action is earnestly solicited.

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